

**THE RENAL SONOGRAPHIC FINDINGS IN HIV/AIDS ADULT PATIENTS
WITH PROTEINURIA AND CD4+ COUNT CORRELATION AT
MWANANYAMALA CARE AND TREATMENT CLINIC**

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**Mmed (Radiology) Dissertation
Muhimbili University of Health and Allied Sciences (MUHAS)**

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By

Silas Napegwa Kishaluli, MD

**A dissertation submitted in (partial) fulfillment of the Requirements for the Degree
of Master of Radiology (Radiology) of
Muhimbili University of Health and Allied Science**

Muhimbili University of Health and Allied Sciences
May, 2013

CERTIFICATION

The undersigned certifies that he has read and here by recommend for acceptance by the Muhimbili University of Health and Allied Sciences a dissertation entitled *Renal sonographic finding in HIV/AIDS adult patients with proteinuria and CD4+ count correlation at Mwananyamala care and treatment clinic , Dar es Salaam ,Tanzania,* in (partial) fulfillment of the requirements for the degree of Master of Medicine (Radiology) of the Muhimbili University of Health and Allied Sciences.

Dr Ramadhan R. Kazema

(Supervisor)

Date _____

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ABSTRACT

Objective: To determine renal sonographic findings in HIV/AIDS adult patients with proteinuria and CD4+ count correlation at Mwananyamala CTC clinic, from July to December 2012.

Methods: This was a cross-sectional study which evaluated 152 patients with HIV/AIDS. These patients underwent right kidney sonography, urinalysis for proteinuria and leukocyte estimation, Renal cortical echogenicity was graded using Hricak standardized scoring method. Patients not consented, HIV negative, CD4+ count taken within three months, hypertension, Diabetic mellitus, chronic kidney diseases, cardiac disease and infection of urinary tract were excluded from the study. The patients were recruited from HIV/AIDS clinic (CTC) from July 2012. A systemic random sampling was used. Most current CD4+ count of not more than three months was taken from patients' file. Renal cortical echogenicity, CD4+ count, and proteinuria were analyzed for correlation.

Results: This study shows that there is high significant association between level of proteinuria and renal echogenicity appearance in HIV/AIDS adult patients 4($P<0.001$). There is significant relation between right renal length and level of proteinuria in HIV/AIDS patients ($p<0.001$). This study also revealed that there is no relation between right renal length and level of CD4+count($P=0.982$) the study revealed also patients with higher CD4+ counts had renal echogenicity grade III however there was no significant association. It was shown that the most frequent renal echogenicity was normal renal length??

Conclusions: The following were observed:

1. The level of proteinuria and the renal length can be used as good indicator for renal parenchymal disease in HIV/AIDS patients.
2. There is no relation between level of CD4+ count and renal sonographic appearance.
3. The most frequent renal echogenicity is .

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LIST OF ABBREVIATION

RMO.....	Regional Medical Officer
DMO.....	District Medical officer
TACAIDS.....	Tanzania Commision for AIDS
HIV.....	Human immune Deficiency Virus
ART.....	Antiretroviral Treatment
GFR.....	Glomerular filtration rate
CTC.....	Care and Treatment Clinic
DHHS.....	Department of Health and Human Services
U.S.....	United States of America
ESRD.....	End-Stage Renal Disease
CKD.....	Chronic Kidney Disease
HIVAN.....	Human Immunocompromise Virus-associated Nephropathy
HERS.....	HIV Epidemilogy Research Study Group
CDC.....	Communicable Disease Control
DHHS.....	Department of Health and Human Services
MHz.....	Megahetz
MUHAS.....	Muhimbili University of Health and Allied Sciences
SPSS.....	Statistical Package for Social Science

1.0 INTRODUCTION AND LITERATURE REVIEW

1.1 HIV PREVALENCE IN TANZANIA

The United Republic of Tanzania has population of about 40 million people, Tanzania is a low-income country experiencing a mature, generalized HIV epidemic, which is still growing. It is estimated that about 5.7% of adults aged between 15 and 49 years (6.6% of women and 4.6% of men) in Tanzania, this is approximately 1.5 million people are currently HIV-infected, approximately 90% of them are adult. (1)

1.2 PREVALENCE OF HIV NEPHROPATHY IN TANZANIA AND WORLDWIDE

Initial reports have suggested that approximately 10% of patients with HIV-infection develop HIV-associated nephropathy (HIVAN). It has also been predicted that by the end of the decade, HIVAN is likely to become a third leading cause of end-stage renal disease (ESRD) in African-Americans between the ages of 20-64 years. (2)

Lack of published literature on HIVAN in Africa include Tanzania is related to multiple factors, including a lack of surveillance and reporting for renal disease[3], therefore assuming the prevalence of HIVAN among black patients in this region is similar to that for HIV-1—infected black patients in the United States, one would predict prevalence of HIVAN in Sub-Saharan Africa include Tanzania to be 10%, (2,3) while other study shows that the prevalence of HIVAN among HIV-infected black patients has been reported to be 3.5% in a cohort

screened for proteinuria in a primary care setting, Study of imaging and histopathologic features of HIV-related renal disease, the autopsy series shows the prevalence of HIV-associated nephropathy in the United States has been reported to be 3%–7% (2,4).

Prevalence of renal dysfunction among HIV patients in Tanzania without risk factors for chronic kidney disease such as hypertension, diabetes mellitus, or hepatitis C infection is 25% for patients with proteinuria or microalbuminuria however the prevalence of renal disease among HIV Infected patients has been reported to be 2 to 10% with about 3.5% from black origin (5,6).

Screening for kidney disease in HIV-infected persons is an important aspect of primary care as early identification of patients with renal dysfunction allows early intervention targeting at reversing the process of renal injury or slowing down its progression (7). In Tanzania we don't have guideline for renal screening however we have HIV/AIDS guideline which insist on evaluation renal status to be done before initiating therapy in any patient, the baseline laboratory tests recommended for renal evaluation is urinalysis and Renal Function Tests (Creatinine , Blood Urea Nitrogen (BUN)) however Serum creatinine could be done if available and no where ultrasound renal scanning was recommended. Routine monitoring (every six months) of full chemistry include renal function should be considered for patients on second-line drugs. (3,7)

The current guidelines in U.S. recommend all patients at time HIV diagnosis to be assessed for existing kidney disease at entry to care, with subsequent screening as indicated by the patient's risk factors by urine analysis for proteinuria and a calculated estimate of renal function (creatinine clearance or glomerular filtration rate [GFR]). A renal function estimate also allows the caregiver to properly prescribe antiretrovirals and other commonly used medications that require renal adjustment (7). Low grade proteinuria may be an easily detectable indicator of early renal dysfunction in HIV-infected patients associated with potentially modifiable risk factors ,it is known now that proteinuria in HIV infected patients is an early marker of HIV associated nephropathy . (8, 9 , 10)

1.3 RISK FACTORS FOR HIV NEPHROPATHY

If you have HIV, you are more likely to develop kidney disease however the following risk factors increase chance of get HIVAN being African American, black , *diabetes* ,*have* high blood pressure , older ,*have* a lower *CD4 count* (below 200 cells/mm³) but it can occur at any CD4 count , *have* a higher *viral load* , *have Hepatitis B or Hepatitis C, and Nephrotoxicity* (2 , 6).

“Nephrotoxicity” is a term that means “toxicity or injury to the kidneys.” For people living with HIV/AIDS, nephrotoxicity can be an adverse side effect of certain HIV medications, including *protease inhibitors* and *nucleoside reverse transcriptase inhibitors* (NRTIs) (4 , 6).

1.4 CAUSES FOR HIV NEPHROPATHY

Patients with HIVAN may or may not have clinical AIDS. Renal involvement in HIV patients may be related to either direct infection of the renal epithelium by the virus postulated to be the cause of HIV nephropathy or drug associated damage as the antiviral drugs are nephrotoxic. Glomerular and tubular epithelial cells have been shown to be selectively infected by HIV-1 (11).

Pathogenesis of HIV associated kidney disorders

The pathogenesis of HIV associated nephropathy is largely unknown. Nephropathy is reported to result from infection of renal epithelial and mesangial cells with HIV in a genetically susceptible host.(12) HIV is reported to enter epithelial cells by three routes which are binding of cell-free virus to specific receptors, fusion with infected mononuclear cells and direct transfer on intimate contact between infected mononuclear cells and epithelial cells.

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Renal epithelial cells do not express T-cell glycoproteins CD4, CCR5 and CXCR4 which are responsible for HIV-1 entry, instead HIV-1 uses other chemokine receptors for infection such as chemokine C-C motif ligand 3 (CCL3) or Duffy antigen receptor complex.[12] Infection of podocytes and mesangial cells with HIV induce an inflammatory response with expression of cytokines (TNF α , IL-2, and IFN- γ), growth factors (PDGF, TGF- β , and FGF-2), chemokines and adhesion molecules (.15 , 16 , 17)

Inflammatory mediators released following HIV-1 infection result in a combination of pathologic changes in the renal tissues including sclerosis and apoptosis. Infection of podocytes with HIV is postulated to induce these structures to de-differentiate and proliferate resulting in glomerular capillary collapse.(18 , 17) Deposition of immune complexes in the renal tissues as a result of interaction between circulating immunoglobins with HIV are also reported to contribute in renal pathology. (19)

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1.5 INVESTIGATION OF THE CAUSES OF HIV NEPHROPATHY

HIVAN is now being recognized as a distinct clinico-pathological entity that presents with proteinuria in the nephrotic range and impairment of renal function. Side effects due to anti-HIV drugs are many. They include hepatotoxicity and nephrotoxicity (23 , 48).

Diabetes when fast blood glucose is greater than 3.9-5.6g/dl or random blood glucose is greater than 11.1g/dl and hypertension (at least 140/90) are the two leading causes of CKD in the United States. Patients with known diabetes, particularly those with retinopathy and with pre-existing proteinuria, can usually be assumed to have diabetic nephropathy and confirmed by blood glucose level. (23 , 24).

Patients with long-standing hypertension which is measured by blood pressure machine, low grade proteinuria (< 1 gm/day) and urine sediment without cells or casts which measured by urine dip stick(urinalysis) may be assumed to have hypertension as the cause of their kidney disease (23 , 24).

Serum anti-nuclear antibody, anti-neutrophil cytoplasmic antibody, complement levels, hepatitis B and C virus antibodies, syphilis serology (if a biopsy is contemplated) can be useful in identifying when kidney disease may be auto-immune related or potentially due to HBV, HCV or syphilis (11) .

1.6 USEFULNESS OF SERUM CREATININE, URINALYSIS AND ULTRASOUND

Serum creatinine levels can be used to estimate glomerular filtration rates (GFR) in patients whose levels are in a steady state, and serve as the best marker of kidney dysfunction, used both for staging CKD and recognizing acute kidney infection (25) .

Urinalysis is the early and accurate assessment of proteinuria is a critical aspect in the detection and management of kidney disease in people living with HIV (8) . Urinary dipstick tests yield qualitative results. “Usually, if there is more than 2g/day (~ 2+ on a dipstick) of proteinuria, the kidney disease is glomerular. Anything less can come from tubulointerstitial or glomerular disease” . A first morning specimen is preferred, but random urine specimens are acceptable (11) .

Protein concentration dependent on patient hydration or how concentrated the urine sample is. This test can only give a rough indication of the presence or absence of pathological proteinuria, the test only measures albumin and will be falsely negative if

the urine protein is globulin, such as often found in paraproteinemia. The specificity of urinalysis using protein dipsticks for the detection of proteinuria is approximately 67 percent (26, 27).

Patients with HIVAN had more significant proteinuria compared with those without HIVAN, patients with proteinuria of grade > 1+ by dipstick analysis or reduced renal function (GFR, <60 mL/min per 1.73 m²) should be referred to a nephrologist and undergo additional evaluation, including quantification of proteinuria, renal ultrasound, and potentially renal biopsy (38).

Ultrasound can show whether a kidney is normally sized (normal 10-12cm), large, or shrunken or whether there are obstructions in the urinary track. Small kidneys (<9cm) may point towards CKD, “whilst with normal or big kidneys it is difficult to be sure as many HIV related nephropathies cause increased size initially.” The characteristic ultrasound appearance of very echogenic, large kidneys is highly suggestive of HIVAN and probably due to the presence of the large, multiple, hard protein casts in dilated tubules (4, 28).

1.7 ULTRASOUND FEATURES OF HIV NEPHROPATHY

HIV-associated nephropathy (HIVAN) commonly presents with the following sonographic findings: Enlarged, globular kidneys with marked echogenicity in a heterogeneous pattern, loss of corticomedullary definition, and obliteration of renal

sinus fat. These findings may be more prominent in setting of clinical AIDS. HIV-positive patients may have HIVAN according to diagnostic criteria but still have few if any of the classic sonographic signs. (28)

The characteristic feature of HIVAN is the increase in renal echogenicity. This may manifest as patchy or spotty increase in echogenicity. Advanced stages of HIVAN typically demonstrate a diffuse increase in renal echogenicity, Pelvi-calyceal thickening. (28, 29)

The characteristic ultrasound appearance of very echogenic, large kidneys is highly suggestive of HIVAN and probably due to the presence of the large, multiple, hard protein casts in dilated tubules. The differential diagnosis for this ultrasound appearance is other causes of cast nephropathy such as myeloma, crystalluria causing tubular obstruction or infiltration with amyloid or lymphoproliferative disorders (32). Large, brightly echogenic kidneys in black patients . with renal failure is suggestive of HIV associated nephropathy. Advanced stages of HIVAN may also show A globular renal configuration, Decreased renal sinus fat, decreased cortico-medullary differentiation and parenchymal heterogeneity (28 , 32).

1.8 ROLES OF COMBINATIONS OF RENAL ECHOGENICITY AND RENAL LENGTH IN HIV NEPHROPATHY

Renal echogenicity graded according to a standardized score with 4 categories i.e grade 0e renal cortex is less echogenic than the liver , grade I the renal cortex and liver are equally echogenic , grade II the renal cortex is more echogenic than the liver , grade III the renal cortex and renal sinus are equally echogenic (38 , 48).

Ultrasound examination was carried out prospectively on 120 HIV-infected patients renal sizes were normal in 85%, small in 7%, and large in 8% of patients. Fifty patients (41.7%) had increased renal echogenicity and 8 (6.7%) had severe increased echo-texture while seventy (58.3%), 16 (13.3%), 26 (21.7%), and 8 (6.7%) patients had normal, grade I, II, and III echogenicity ,(29 , 38 , 48).

In one of study report shows the renal sonographic (using the reflections of high-frequency sound waves to construct an image of a body organ) findings in 76 patients with HIV, the largest series to be reported. In this study. 30 kidneys (20%) were enlarged. Fifty-six patients (74%) had cortical echogenicity greater than that of the liver or spleen; patients (16%) had equal echogenicity and 20% of patients in their series had kidneys larger than 13cm and 58% of patients had kidneys that were of echogenicity equal to or greater than that of the liver .spleen. or both (23, 29 , 30 , 48).

Only 8% of the patients had enlarged kidneys. This low prevalence of enlarged kidneys in HIV/AIDS is consistent with the findings of other workers who reported an 11%-20% prevalence of enlarged kidneys in HIV-infected patients (29).

There were significantly more patients with renomegaly and increased renal echogenicity than those patients with normal-sized kidneys and increased renal echogenicity (53.6% v. 33.6%, $p=0.006$). (29 , 31).

Highest level of echogenicity based on a standardized measure is a strong predictor of HIVAN, and the lowest levels of renal echogenicity may be useful in excluding the diagnosis of HIVAN. Found no difference in kidney size based on HIVAN status (32).

The size and echogenicity of the kidneys may help differentiate acute and chronic kidney disease., Small and echogenic kidneys with bipolar renal length smaller than 9 cm suggest chronic renal failure, though HIV, diabetes, and some other chronic conditions are associated with normal size or large kidneys, Large, brightly echogenic kidneys in black patients . with renal failure is suggestive of HIV associated nephropathy, increased renal sizes and degree of echogenicity alone are not useful predictors of renal involvement in HIV/AIDS (23 , 28 , 29)

1.8 EFFECT OF PROTEINURIA AND RENAL LENGTH IN HIV NEPHROPATHY AND THEIR RISK FACTORS

Proteinuria in HIV infected patients is an early marker of abnormal kidney function and should be assessed in all patients for HIV associated nephropathy and is a major determination of progression of renal disease . HIV positive patients show that proteinuria is associated with a double in the risk of death (33 , 34 , 35 , 36).

Nearly a third (33%) of HIV-positive individuals maintain high levels of protein in the urine, very small amounts of protein are normally excreted in the urine. persistently increased protein excretion is a marker of kidney damage and one of the diagnostic criteria for CKD (37 , 38).

Features of renal involvement include proteinuria, urinary casts, fluid and electrolyte disorders and enlarged echogenic kidneys on ultrasound. Nephrotic range proteinuria has been reported with a prevalence of 7% and 13% of HIV-1 infected adults and children respectively, prevalence of grade 1+ proteinuria by dipstick analysis of urine, a marker for glomerular disease, is approximately 30%, (4, 38 , 39).

In a study involving HIV infected outpatients and healthy (HIV negative) controls by urinalysis results were normal in almost all the participants. However, 38 people (11.55% of the population) had proteinuria values 30 mg/dL, while 21(6.38%) had proteinuria values > 30 mg/dL, 4(1.22%) had proteinuria greater than or equal to 30 mg/dL, and 2(0.61%) had significant Proteinuri . Leukocytes were found in urine of 4(1.22%) subjects out of which

2(0.61%) had significant proteinuria and patients with leukocytes greater than 10 wbc/hpf were considered to have UTI (23 , 28 , 29, 39) .

Up to 30% of HIV positive individuals may have protein in their urine . Given the prevalence of proteinuria in Western cohorts of 14 to 32% as opposed to significant proteinuria seen in 8.3% of the HIV infected participants and leukocytes were found in the urine samples of 2 who had significant proteinuria; this is evident of bacterial infection, which may not necessarily lead to a reduction in renal function except it is left untreated (23 , 40) .

The study to determine whether renal sonography can be used to predict the pathologic diagnosis of human immunodeficiency virus-associated nephropathy and study shows that patients with HIVAN had more significant proteinuria compared with those without HIVAN (32) .

In HIV patients. the average length of the right kidney was 11.6 cm and of the left was 11.5 cm: On the basis of length.30 kidneys (20%) six of HIV patients and 24 of AIDS patients, were considered large (37) .

1.9 EFFECT OF PROTEINURIA AND RENAL ECHOGENICITY IN HIV NEPHROPATHY

The most common abnormality in patients with HIV-related renal disorder is a highly echogenic renal cortex and the highest level of renal echogenicity has been reported to be suggestive of a diagnosis of HIVAN, particularly in cases where renal biopsies cannot be done or are contraindicated (32).

Proteinuria was present in some HIV/AIDS patients, this parameter alone is not indicative of HIVAN, HAART improve patient outcome by reducing patient's susceptibility to kidney disease. Cotrimoxazole therapy though beneficial, affects GFR and cause proteinuria therefore should be administered with care to these patients if not eliminated from their drug regimen (23).

1.10 EFFECT OF CD4 COUNTS ON HIV NEPHROPATHY

Apart from renal function test which is used to estimate renal status the degree of immunodeficiency is related to the level of the CD4+ count which also is a good indicator for monitoring the disease's progression. It is expected that, as CD4+ count decreases, susceptibility to infection and consequently abnormal renal sonographic findings increase(7). HIVAN is almost exclusively seen in black patients and can occur at any CD4count. Ongoing viral replication appears to be directly involved in renal injury, and HIVAN is extremely

uncommon in virologically suppressed patients. ART in patients with HIVAN has been associated with both preserved renal function and prolonged survival as it increase CD4+ counts.(38 , 40 , 42 , 43)

1.12 EFFECT OF CD4 COUNTS AND RENAL LENGTH IN HIV NEPHROPATHY

HIVAN Is the most common form of renal disease in HIV patients with a CD4+ < 200 cells/ μ l this is because HIV opportunistic infections are highly common in patients with CD4+ < 200 cells/ μ l in that case HIV remains an important risk factor for the development of end stage renal disease (ESRD) which pointed toward small kidney (4 , 28 , 44 , 45).

Therefore degree of immunodeficiency is related to the level of the CD4+ count and, as such, CD4+ count is a good index for monitoring the disease's progression , due to this it is expected that, as immune status decreases ,susceptibility to infection and consequently abnormal renal sonographic findings should increase (24).

Patients with CD4 cell counts < 200 cells/mm³ have an increased risk of HIV-related renal diseases, small kidneys(<9cm) may point towards chronic kidney disease, “whilst with normal or big kidneys(e.g., > 13 cm) it is difficult to be sure as many HIV related nephropathies cause increased size initially.” Can be seen in diabetes, amyloid, infiltrative diseases and HIV-associated nephropathy (HIV-AN) however normal size indicates kidney disease that may be amenable to medical treatment. (11 , 23 , 38)

There was significant negative correlation between renal length and measured CD4 cell count ($p < 0.01$), Study of trans-abdominal ultrasonic findings correlated with CD4+ counts in adult HIV-infected patients, renomegaly seen in 56 (18.7%) patients, without significant correlation with their CD4+ counts. from these cases of renal enlargement, 11 (19.6%) had right-sided renomegaly only (31 , 39).

AIDS Patients with CD4 $< 200/mm^3$ result shows that patients with normal renal size were 70 (94.6%), small size where 1(1.4%), large size where 3(4.1%) and those patients with CD4 200-499/ mm^3 result showed that patients with ,normal renal size where 30(83.3%),small size where 4(11.1%) ,large size 2(5.6%), in the last group of CD4 $> / 500$ count patients with normal renal size where 6(100%,small and large size was 0(0%) (29).

1.13 EFFECT OF CD4 COUNTS AND RENAL ECHOGENICITY IN HIV NEPHROPATHY

Renal parenchyma should be isoechogenic or hypoechogenic when compared with that of the liver and spleen; hyperechogenicity indicates diffuse parenchymal disease (23).

The characteristic ultrasound appearance of very echogenic, large kidneys is highly suggestive of HIVAN and probably due to the presence of the large, multiple, hard protein casts in dilated tubules. Large, brightly echogenic kidneys in black patients . with renal failure is suggestive of HIV associated nephropathy. Small echogenic kidneys (< 8 cm) suggest irreversible disease (23 , 27)

The distribution of echogenicity scores was as follows: (renal echogenicity greater than liver) grade 0, 6.5%; grade I, 25.8%; grade II, 48.4%; and grade III, 19.4% this shows that almost 50% of HIV-positive patients had an echogenicity score of II, Human immunodeficiency virus-associated nephropathy was the most common pathologic diagnosis, this grade of renal echogenicity described in Text book of Radiology and Imaging (40.3%) (38, 48).

Of 152 kidneys imaged, sonography showed abnormal echogenicity was present in 136 kidneys (89%). Increased parenchymal echogenicity at US is the most characteristic feature of HIV-associated nephropathy, It may manifest as patches of increased echogenicity and has been reported to occur in up to 89% of patients with HIV-associated nephropathy, normal echogenicity in 58.3% of patients studied compared with 42% of their study population had normal echogenicity (2, 29, 38, 46, 48).

Despite the finding that more than half of the patients in this study had CD4⁺ cell counts < 200 cells/mm³, and therefore highly immunocompromised and likely candidates for development of HIVAN, only a small proportion (6.7%) had markedly increased echogenicity. This finding of normal echogenicity in 58.3% of patients studied compared with 42% of study population of another study had normal echogenicity shows no significant relationship or correlation was found between CD4⁺ cell counts and renal echogenicity (30, 29, 38, 47).

Patients with CD4 <200/mm³ result shows that patients with normal echogenicity where 40(34.5%) and increased renal echogenicity where 34(29.3%) patients, those with CD4 200-499/mm³ result showed that patients with normal echogenicity where 27(23.3%) and increases renal echogenicity where 9(7.8%) patients where as in the last CD4+ > 500/mm³ the patients with normal and increased echogenicity where 6 (3.3%) patients each (29).

Normal renal echogenicity was seen in 188 (62.7%) patients, while 112 (37.3%) patients had varying grades of renal echogenicity this finding shows that patients with depleted CD4+ had a higher proportion of increased cortical echogenicity. No significant correlation between renal echogenicity and CD4 cell count was noted (2 , 31 , 48).

2. PROBLEM STATEMENT

Lack of published literature on HIVAN in Africa include Tanzania is related to multiple factors, including a lack of surveillance and reporting for renal disease, screening for kidney disease in HIV-infected persons is an important aspect of primary care as early identification of patients with renal dysfunction allows early intervention targeting at reversing the process of renal injury or slowing down its progression (3 , 7).

In Tanzania we don't have guideline for renal screening however we have HIV/AIDS guideline which insist on evaluation renal status to be done before initiating therapy in any patient and urinalysis is recommended while Renal Function Tests (Creatinine , Blood Urea Nitrogen (BUN)) is recommended only where available and no where mentioned for renal sonographic scan. (3 , 7).

Therefore this study aimed to know if trans abdominal renal sonographic findings and level of protein in urine by urinalysis can be used as routine HIV –associated nephropathy screening test as it is cheap and easily available.

3. RATIONALE

More than 20 antiretroviral drugs and drug combinations are now available in Tanzania for HIV/AIDS patient. Doctors need to have an understanding of the pharmacokinetics of antiretroviral medications and the proper dosing of these medications in patients with impaired kidney function because HIV/AIDS patients are a high risk renal disease patients.

Most studies in the HIV/ AIDS found that many HIV-positive patients continue to lose kidney function despite successful antiretroviral treatment. These studies, also found that renal function estimation and CD4+ count are very crucial for efficacy of antiretroviral drugs and monitoring renal disease progress which allows the caregiver to properly prescribe antiretroviral and other drugs by making dosage adjustments as many antiretroviral agents and other drugs are eliminated at least partly through the kidneys.

Based on above narration it is recommended that all patients at time of HIV diagnosis and routine CTC attendances should be assessed for existing kidney, by screening urine for proteinuria ,estimating renal function (creatinine clearance or glomerular filtration rate [GFR]) ,renal sonographic findings and blood for CD4+ count.

Due to lack of published literature on HIVAN in Africa include Tanzania which is related to multiple factors, including a lack of surveillance and reporting for renal disease, screening programme for kidney disease in HIV-infected persons while this is important aspect of

primary care as early identification of patients with renal dysfunction allows early intervention targeting at reversing the process of renal injury or slowing down its progression (3 , 7).

Study aimed to know if trans abdominal renal sonographic findings and level of protein in urine by urinalysis can be used as routine HIV –associated nephropathy screening test as it is cheap and easily available.

4. OBJECTIVE

Broad objective:

To determine renal sonographic findings in HIV/AIDS adult patients with proteinuria and CD4+ count correlation at Mwananyamala CTC clinic, from July to December 2012.

Specific objectives :

1. To determine renal sonographic finding in HIV/AIDS adult patients in correlation with Proteinuria at Mwananyamala care and treatment clinic from July to December 2012.
2. To determine renal sonographic finding in HIV/AIDS adult patients in correlation with CD4+ count at Mwananyamala care and treatment clinic from July to December 2012.

5. METHODOLOGY

Study design

A cross sectional study

Study duration

The study was conducted for six months duration, between July and December, 2012.

Study area description

The study was conducted at HIV/AIDS Care and Treatment clinic at Mwananyamala regional referral Hospital which serve about 9,000 HIV/AIDS patients a year.

Sample size

Obtained by using the following Computed formulae for determination of sample size.

$$n = \frac{Z^2 \times p(1-p)}{\epsilon^2}$$

WHERE

n = required sample size
Z = confidence level at 95% (standard value of 1.96)
p = estimated prevalence (10%)
ε = margin of error at 5% (standard value of 0.05)

Initial reports have suggested that approximately 10% of patients with HIV-infection develop HIV-associated nephropathy (HIVAN) (2),the calculated minimum sample size is found to be 138.Ten percent of the non-respondent is added to the sample size calculated above, hence a minimum sample size to be is 152.

Study population

HIV/AIDS adult patients attendees at Mwananyamala CTC clinic in Kinondoni district, Dar es salaam.

Study sample

All HIV/AIDS adult patients who met the inclusion criteria in the selected health facilities.

Inclusion criteria

Patient who has consented

HIV Positive

CD4 count determined within three months

Aged 16 years and above

Normaltensive

Non diabetic.

Exclusion criteria

Not consented

HIV negative

No CD4+ counts test within three months

Extremely sick patients

Hypertensive

Diabetic patients

Sampling technique

Systematic sampling of the client was done to recruit the participant where by every tenth client was recruited. This was done for a consecutive of 5 months to obtain a sample of 152 patients. If the selected client was not having the inclusion criteria, next client was selected. Randomization was done care full to include new cases and not to repeat patients who have been previously studies, it was checked by asking the patient if she or he has been involved in this study also mark was put at the top of the patients file to avoid over repetition.

DATA COLLECTION

Two research assistants were trained on the objectives of the study, methods of data collection and data collection instruments. Familiarization of the questionnaire was done at Mwananyamala CTC clinic, systematic sampling was done to select participants.

Data was collected using exit structured questionnaire with both open and closed ended questions on getting personal particular and specimen sample collection for laboratory result was applicable.

Demographics (age, sex, and race), co morbid conditions (UTI ,diabetes mellitus and hypertension), and laboratory investigation include urinalysis for proteinuria ,leukocytes, CD4+ count and blood glucose) were collected after renal scanning however urinary protein, urinary leukocytes and blood glucose laboratory work were done by laboratory technician and result was not disclosed until when scan sonographic findings result was out.

The patient was also asked if she or he had history of hypertension or diabetic. Measurement of Blood pressure was done using Digital blood pressure machine estimation of blood glucose was also done. any patients having blood pressure blood pressure above 140/80 was considered as Hypertensive patients (24).

Random blood glucose test was done where by blood glucose level above 11.1mmol/l and above 3.9-5.6 mmol/l for fasting blood glucose was considered as diabetic patient (24).

Every patients given one small sterile bottle to collect urine of about 10-20mls of urine for urinalysis test (protein and leukocytes) where by patients with leukocytes greater than 10wbc/hpf were considered having UTI (23), blood glucose test was done to measure blood glucose and blood pressure was measured in all patients. Patient were then scanned to find any abnormal renal sonographic finding using real-time sono graphic systems and use 3.5-MHz transducers. Multiple sections evaluated renal length and renal cortex echogenicity as part of our standard protocol for renal sonography.

Each patient's sonograms was evaluated prospectively by the Researcher in collaboration with Sonographer then for quality assurance counterchecked by experienced Radiologist in interpreting sonography findings .

Kidneys were considered large when the length exceeded 13cm, normal when length was 9-13cm, and small if length was less than 9 cm (38) .

Renal echogenicity was graded according to a standardized score with 4 categories :-

0= Indicated that the renal cortex is less echogenic than the liver;

I= The renal cortex and liver are equally echogenic;

II= The renal cortex is more echogenic than the liver;

III= The renal cortex and renal sinus are equally echogenic.

Grading was performed for the right kidney only, and the echogenicity was presumed to be similar bilaterally(38 ,48).

Lastly patients CD4+ count results were traced in the patients file or database room and only CD4+count result which were most current or those done in less than three months from day of interview were included and grouped in three group CD4+ count group:-

1. $<200 \text{ cells/mm}^3$
2. $200 - 499 \text{ cells/mm}^3$
3. $>/ 500 \text{ cells/mm}^3$

DATA ANALYSIS

Data was analysed by using SPSS software program.

ETHICAL CLEARANCE & CONSIDERATION

Ethical clearance was obtained from MUHAS-IRB (Institutional Review Board) and permission to conduct the study was sought from RMO-Dar es salaam and DMO Kinondoni distric.

Explanation was given to the participants on the objectives of the study and that all the information provided is confidential. Participants were ensured that data collected will be used for research only.

Both verbal and written consent was included in the study. To ensure confidentiality, participant`s names were not written on the questionnaires.

Participation to the study was voluntarily and a participant was free to withdraw from the study at anytime when he or she feels so but no one was withdrew from study.

Also the contact address was given to participants in case of any clarification or concern about the study.

Operational definitions

HIV/AIDS ADULT PATIENTS are those patients who are HIV positive ,enrolled in CTC clinic and aged 18-60 years.

Nephrotoxicity is a term that means toxicity or injury to the kidneys(2).

Sonography - Using the reflections of high-frequency sound waves to construct an image of

a body organ(48)

ECHOGENICITY is the ability to bounce an echo (48).

RENOMEGALLY kidney length of more than 13 cm (38)

SMALL KIDNEY kidney length is equal or less than 9cm (38)

HYPERTENSION this is when the reading is at least 140/90 (24).

UTI diagnosed when white blood cells(leukocytes) in urine in greater than 10 wbc/hpf (23)

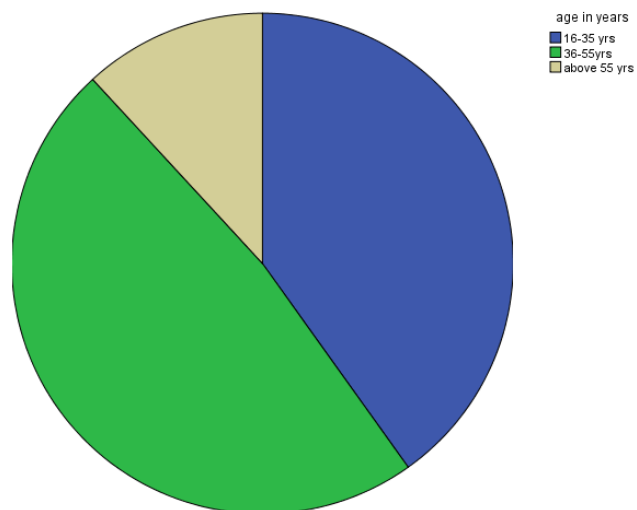
DIABETIC when normal fasting blood glucose range is 70-100 mg/dL (3.9-5.6 mmol/L) or random blood glucose after meals less than 197 mg/dL (11.1 mmol/L) (24).

FAST BLOOD GLUCOSE is blood sugar after not feed for eight hours (24).

RANDOM BLOOD GLUCOSE is blood sugar after recent meals (24).

RESULTS:**DEMOGRAPHICS AND CLINICAL CHARACTERISTICS:****Table 1:0 Age in years distribution(n=152)**

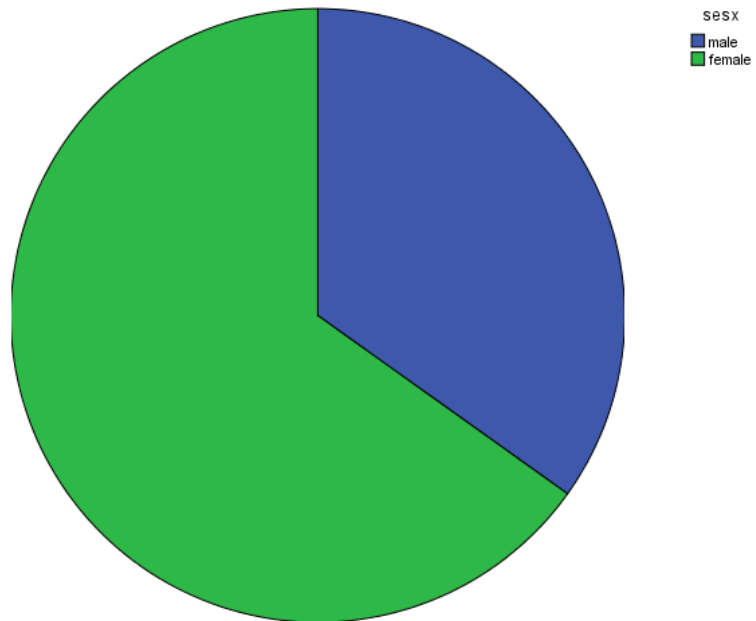
Years	Frequency	Percent	Valid Percent	Cumulative Percent
16-35 yrs	61	40.1	40.1	40.1
36-55yrs	73	48.0	48.0	88.2
above 55 yrs	18	11.8	11.8	100.0
Total	152	100.0	100.0	

Figure 1:0 Age in years distribution (n=152)MMMM

A total of 152 eligible patients consented to participate in the study, most participants were belong to age group 36-55yrs contribute (48.1%) .

Table 2:0 Sex distribution(n=152)

Sex	Frequency	Percent	Valid Percent	Cumulative Percent
male	53	34.9	34.9	34.9
female	99	65.1	65.1	100.0
Total	152	100.0	100.0	

Figure 2:0 Sex distribution

Most of the participants were female who accounted for 65.1%, where as males accounted for 34.9%

MOST FREQUENT RENAL SONOGRAPHIC APPEARANCE

Table 3:0 Frequency grade of right kidney echogenicity

Grade of renal echogenicity	Frequency	Percent
0	134	88.2
I	14	9.2
II	3	2.0
III	1	7.0
Total	152	100.0

Renal echogenicity grade is 0 accounted for 134 (88.2%) .

Table 4:0 Frequency of right kidney length distribution

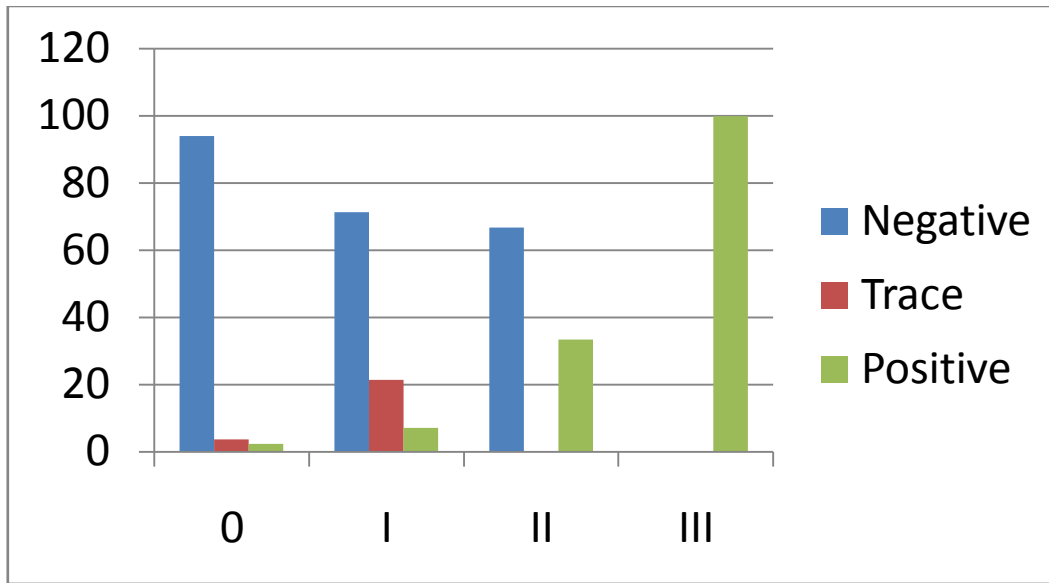
Length of right kidney	Frequency	Percent
< 9 cm	23	15.1
9-13 cm	129	84.9
Total	152	

Normal renal length accounted for 129 (84.9%) and small renal length was 23 (15.1%)

Table 5:0 Grade of kidney echogenicity Vs Level of protein in urine(n=152)

Grade of kidney echogenicity	Level of protein in urine			
	Negative	Trace	Positive+	Total
0	126 94.0%	5 3.7%	3 2.2%	134 100.0%
I	10 71.4%	3 21.4%	1 7.1%	14 100.0%
II	2 66.7%	0 0.0%	2 33.3%	3 100.0%
III	0 0.0%	0 0.0%	1 100.0%	1 100.0%
Total	138 90.8%	8 5.3%	6 3.9%	152 100.0%

Most of patients had no proteinuria

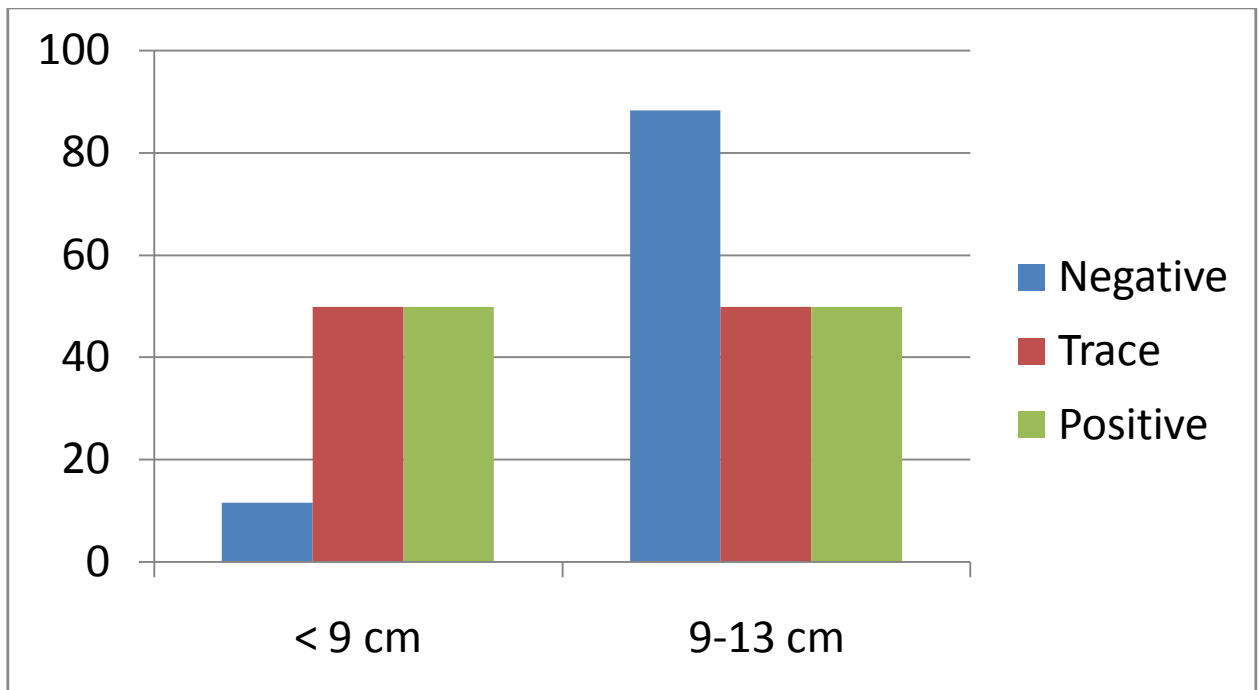
Fig 3:0 Grade of kidney echogenicity Vs Level of protein in urine(n=152)

The percentage of proteinuria increase with increase of grade of right kidney echogenicity and reach maximum in grade III level of echogenicity.

Table 6:0 Right kidney length Vs Level of protein in urine (n=152)

Length of Right Kidney	Level of protein in urine			
	Negative	Trace	Positive+	Total
< 9cm	16 11.6%	4 50.0%	3 50.0%	23 15.1%
9-13 cm	122 88.4%	4 50.0%	3 50.0%	129 84.9%
Total	138 100.0%	8 100.0%	6 100.0%	152 100.0%

Negative proteinuria was most common in patients with renal length of 9-13 cm (88.4 %) and proteinuria was more common in patients with renal length less than 9 cm (11.6 %)

Figure 4:0 Right kidney length Vs Level of protein in urine (n=152)

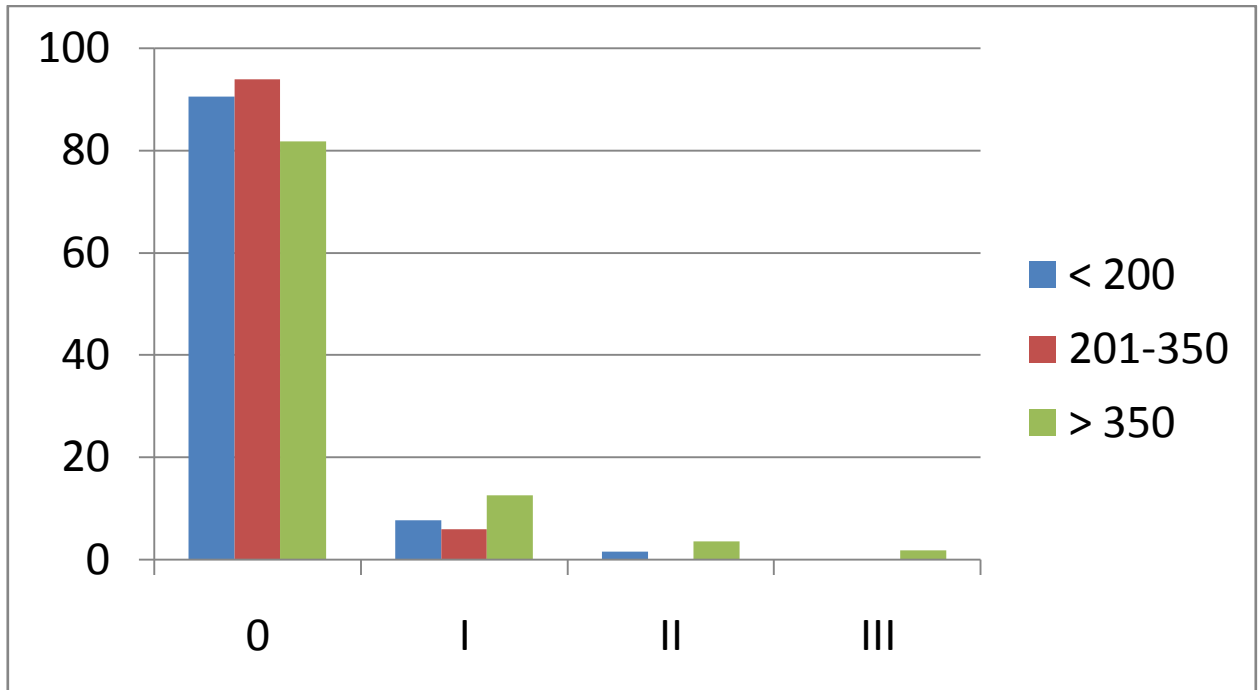
Negative proteinuria was most common in patients with renal length of 9-13 cm and proteinuria was more common in patients with renal length less than 9 cm

Table 7:0 Kidney echogenicity Vs Level of CD4+ count

Grade of echogenicity	Level of CD4 Count			
	<200	201-350	>350	Total
0	58 90.6%	31 94.0%	45 81.8%	134 88.1%
I	5 7.8%	2 6.0%	7 12.7%	14 9.2%
II	1 1.6%	0 0.0%	2 3.6%	3 1.9%
III	0 0.0%	0 0.0%	1 1.9%	1 0.08%
Total	64 100.0%	33 100.0%	55 100.0%	152 100.0%

Show in Grade 0 level of echogenicity there is high frequency of patients with CD4+ < 200, 201-350 and >350

Figure 5:0 Kidney echogenicity Vs Level of CD4+ count



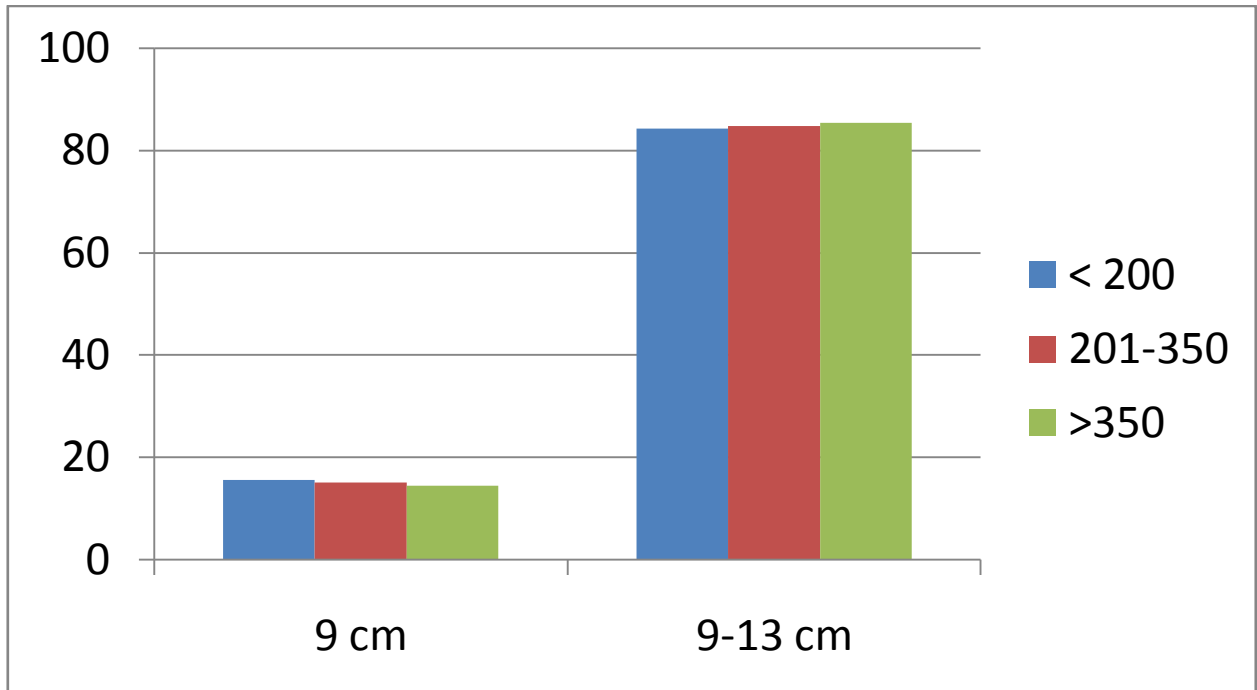
Shows in Grade 0 level of echogenicity there is high frequency of patients with CD4+ < 200, 201-350 and >350

Table 8: Right kidney length Vs Level of CD4+ count(n=152)

Length of right Kidney	Level of CD+ Count			Total
	<200	201-350	>350	
< 9cm	10 15.6%	5 15.1%	8 14.5%	23 15.1%
9-13 cm	54 84.4%	28 84.9%	47 85.5%	129 84.9%
Total	64 100.0%	33 100.0%	55 100.0%	152 100.0%

There is almost equal frequency of find patients with CD4+ count < 200, 201-350 and > 350 in group of patients with right renal length of 9cm and that of 9-13cm

Figure 6:0 Right kidney length Vs Level of CD4+ count



There is almost equal frequency of find patients with CD4+ count < 200, 201-350 and > 350 in group of patients with right renal length of 9cm and that of 9-13cm

DISCUSSION

This study revealed that there is no relation between grade of renal echogenicity and level of CD4+ count ($P=0,558$) by showing that in grade 0 level of renal echogenicity there is high frequency of patients with all groups of CD4+ counts i.e CD4+ < 200, 201-350 and >350 and also revealed that there is no relation between length of renal and level of CD4+ count ($P<0.987$) by showing that there is equal chance of finding patients with CD4+ count < 200, 201-350 and > 350 in group of patients with right renal length of 9cm and equal chance of finding patients with CD4+ count < 200, 201-350 and > 350 in group of patients with right renal length of 9-13cm.

Therefore this study revealed that there is no relation between level of CD4+ cell count, renal length and renal echogenicity, The same finding seen in other studies that no significant correlation between renal echogenicity and CD4 cell count and there is negative correlation between renal echogenicity and CD4+ counts (4, 28 , 29 , 39 , 48).

This study shows that there is very high significant relation between increase level of protein in urine and increase renal echogenicity appearance in HIV/AIDS adult patients($P=000$) *as this study shows that* The level and chance of getting patients with proteinuria increase with increase of grade of right kidney echogenicity and it reach its maximum in grade III level of renal echogenicity this is similar to other study finding like persistently increased protein excretion is a marker of kidney damage and one of the diagnostic criteria for CKD and highest

level of echogenicity strong predictor of HIVAN, and the lowest levels of renal echogenicity may be useful in excluding the diagnosis of HIVAN (32 , 37).

This study shows that there is significant relation between right renal length and negative level of proteinuria in HIV/AIDS patients, $P= 0.001$ by shows that negative proteinuria was most common in patients with normal renal length and proteinuria was more common in patients with small renal simila finding shows that proteinuria in HIV infected patients is an early marker of HIV associated nephropathy[33,34] and is a major determination of progression of renal disease as persistently increased protein excretion is a marker of kidney damage and one of the diagnostic criteria for CKD while patients with CKD have small kidney (28 , 32 , 35 , 37 ,38).

LIMITATION OF STUDY

Scarcity of fund caused by fluctuation of running cost for research

Is hospital based study,results not generalizable to community level.

During study period there were times when ultrasound machine was busy for other normal routine scan business patients complain for long stay waiting for scanning.

CONCLUSION

There is significant correlation between level of proteinuria and length of renal(P<0.001) also there is significant relation between kidney echogenicity and level of proteinuria (P<0.000) the study demonstrated that there is no correlation between level of CD4+ count, kidney echogenicity and right kidney length (P<0.558 Vs P<0.987) , The most frequent renal sonographic finding in HIV/AIDS patients is normal right and left renal length.

RECOMMENDATIONS

Urinalysis for proteinuria and Transabdominal renal sonographic scan should be considered in renal screening test in HIV/AIDS patients.

There is a need for the same study to be done in community based study focusing on those HIV/AIDS patients on ARV drugs and those who not ARV drugs in big sample size.

There is a need for the same study to be done in community based study focusing on sensitivity and specificity of transabdominal renal sonographic appearance and urinalysis for proteinuria in big sample size.

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QUESTIONNERS

1 .Patient number.....

2. Age

3. Sex.....

4. Resident.....

5. Are you known diabetic patients

1/ Yes

2/ No

6. If NO in question Na. 5 take blood sample for Rapid blood glucose , is the blood
glucose lever suggest Diabetic disease

1/ 3.5-11 mmol/l (Random blood sugar)

2/ 3.5-6.5 mmol(fast blood sugar)

3/ >12mmol/l (Random blood sugar)

4/ >8 mmol/l (fast blood sugar)

5 .Are you known Hypertensive patients

1/ Yes

2/ No

6 .If the answer is NO in question Na.6 take Blood pressure measurement.

1/ <135/85mmHg (Norma tensive)

2/ >135/85 mmHg (Hypertensive)

7 .What is patient protein level in urine.

0/ Negative

1/ Negative-Trace (<30mg/dl)

2/ Positive +(30-100mg/dl)

3/ Positive ++(100-300mg/dl)

4/ Positive +++(300- 2000mg/dl)

5/ Positive++++(>2000mg/dl)

8. Is there any leukocytes in urine.

1/ Yes

2/ No

7. What is renal echogenicity result

1/ 0(Renal cortex was less echogenic than the liver)

2/ I (Renal cortex and liver were equally echogenic)

3/ II (Renal cortex was more echogenic than the liver)

4/ III (Renal cortex and renal sinus were equally echogenic)

8. What other renal finding

0/ No

1/ Patch of echogenic

2/ Cyst

3/ Dilatation of Calyx

9. What is sonographic length of right kidney

1/ 9-13 cm

2/ < 9 cm

3/ > 13 cm

10. What is the most current CD4+ count result(not more than three months from now)

a) <200 cells/mm³

b) 200 - 499 cells/mm³

c) > 500 cells/mm³

DODOSO

- 1 .Namba ya mgonjwa.....
- 2.Umri
3. Jinsia.....
4. Makazi ya kudumu.....
5. Je wewe ni mgonjwa unayejijua wa kisukari
 - 1/ Ndio
 - 2/ Hapana
6. Kama jibu la Na.5 ni Hapana chukua damu na pima wingi wa sukari katika damu.
 - 1/ 3.5-11.1 mmol/l (Saa 1-5 baada ya kula)
 - 2/ 3.5-6.5 mmol (masaa 8 baada ya kula)
 - 3/ >12 mmol/l (Chini ya masaa 8 baada ya kula)
- 5 .Je wewe ni mgonjwa unayejijua wa presha ya kupanda
 - 1/ Ndio
 - 2/ Hapana

6 .Kama jibu ni hapana katika swali Na. 6,pima presha ya mgonjwa.

1/ <140/80mmHg(presha kawaida)

2/ >140/80 mmHg(presha juu)

7 .Nini kiwango cha protein katika mkojo?

0/ Hakuna

1/ kidogo (<30mg/dl)

2/ Chanya +(30-100mg/dl)

3/ Chanya ++(100-300mg/dl)

4/ Chanya +++(300- 2000mg/dl)

5/ Chanya++++(>2000mg/dl)

8. Je kuna chembe hai za damu nyeupe kwenye mkojo?

1/Ndio

1/ Hapana

7. Nini kiwango cha ung`avu cha figo?

1/ 0(Kiwango cha ung`avu wa koteksi ni mdogo kuliko ung`avu wa Ini)

2/ I (Kiwango cha ung`avu wa figo koteksi na Ini unalingana)

3/ II (Kiwango cha ung`avu wa koteksi cha figo ni kikubwa kuliko cha Ini)

4/ III (Kiwango cha ung`avu cha koteksi na sinasi cha figo vinalingana)

8. Jambo gani lengine lililoonekana kwenye figo

0/ Hakuna

1/ Mabaka ya ung`avu

2/ Uvimbe uliojaa kimiminika.

3/ Kutanuka kwa kaliksi

9. Nini muonekano wa urefu wa figo la kulia.

1/ 9-13 cm

2/ < 9 cm

3/ > 13 cm

10. Nini kiwango cha sasa cha CD4+(kisiwe cha zaidi ya miezi mitatu tokea leo)

a) <200 cells/mm³

b) 200 - 499 cells/mm³

c) > 500 cells/mm³